Off-Label Promotion: Will the Government Take the First Amendment Seriously?

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Overview

• Legal Framework
• Aggressive Enforcement
• Legal Challenges to the Government’s Stance
• The Government’s Post-\textit{Caronia} Approach
• First Amendment Principles
• The Path Forward
Legal Framework
Federal Food, Drug, and Cosmetic Act

• Regulates:
  – Labeling
  – Advertisements

• Prohibits:
  – Adulteration
  – Misbranding

• Criminal penalties:
  – Strict liability misdemeanor
  – Felony if fraud or recidivism
Labeling and Advertisements

• Labeling:
  – All written, printed or graphic material "(1) upon any [drug or device] or any of its containers or wrappers, or (2) accompanying such [drug or device]” (21 U.S.C. § 321(m))

• Advertisements:
  – Not defined in the FDCA or regulations
  – Appear “in published journals, magazines, other periodicals, and newspapers, and advertisements broadcast through media such as radio, television, and telephone communication systems” (21 C.F.R. § 202.1(l)(1))
Misbranding

• A drug shall be deemed to be misbranded:
  – “If its labeling is false or misleading in any particular” (21 U.S.C. §352(a))
Prohibition on Off-Label Promotion in Labeling

• The safety or efficacy of an off-label use for a drug may not be “prescribed, recommended, or suggested in the labeling thereof” (21 U.S.C. §321(p))

• No statutory prohibition on off-label promotion outside of labeling
“Intended Use”

“The objective intent of the persons legally responsible for the labeling of drugs”

(21 C.F.R. § 201.128)

• Intent determined by the person’s “expressions” and “the circumstances surrounding the distribution of the article” such as:
  – “labeling claims, advertising matter, or oral or written statements by such persons or their representatives”
Is Knowledge of Off-Label Use a Crime?

• “If a manufacturer knows, or has knowledge of facts that would give him notice, that a drug . . . is to be used for conditions, purposes, or uses other than the ones for which he offers it, he is required to provide adequate labeling for such . . . uses to which the article is to be put.”

(21 C.F.R. § 201.128)
But No Way to Provide Adequate Directions for Off-Label Use

- Speech about off-label use makes that use “intended”
- Manufacturer then is required to provide “adequate directions” for that use
- But manufacturer is forbidden from doing so
Result: Chill of off-label speech
The False Claims Act

• How does truthful speech about an off-label use transform a truthful claim seeking reimbursement for that use into a “false or fraudulent claim?”
OIG Exclusion

- Offense “relating to fraud, theft, embezzlement, breach of fiduciary responsibility, or other financial misconduct” (42 U.S.C. § 1320a-7(a),(b))

- Exclusion from participation in a federal healthcare program:
  - Mandatory for a predicate felony
  - Discretionary for a predicate misdemeanor
Aggressive Enforcement
Record-Breaking Recoveries
Enforcement Actions
Legal Challenges to the Government’s Stance

“It is emphatically the province and duty of the judicial department to say what the law is.”

- Marbury v. Madison (1803)

• “In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe.”

13 F. Supp. 2d at 67

• “To endeavor to support a restriction upon speech by alleging that the recipient needs to be shielded from that speech for his or her own protection, which is the gravamen of FDA's claim here, is practically an engraved invitation to have the restriction struck.”

13 F. Supp. 2d at 70
Allergan v. United States (2009)

FDA “has promulgated a series of overlapping and interlocking regulations that combine to render unlawful virtually all manufacturer communication, through any avenue, to any audience, about the lawful off-label use of a prescription drug.”
Allergan v. United States (2009)

1. “Under the ‘intended use’ regulations . . . any affirmative manufacturer communication about an off-label use . . . would arguably demonstrate the manufacturer’s ‘intent’ to sell the drug for that off-label use.”

2. “[T]herefore, a manufacturer that speaks about an off-label use thus must provide ‘adequate directions’ for that off-label use in the drug’s ‘labeling.’”

3. “The manufacturer cannot, however, lawfully alter the ‘labeling’ of a drug to provide ‘adequate directions’ for an off-label use. Such a modification to a drug’s FDA-approved ‘labeling’ would transform the drug into a ‘new drug’ that cannot be sold.”
Allergan v. United States (2009)

• The Government often highlights dangers of off-label use, but:
  – Congress determined that, on balance, benefits of lawful off-label use outweigh its costs.
  – Congress recognized that off-label uses can be “medically accepted” and critical to appropriate patient care, and thus requires taxpayer reimbursement.
Allergan v. United States (2009)

- Declaratory action dismissed as a condition of Allergan’s settlement with the Department of Justice in 2010.
Par Pharmaceutical v. FDA (2011)

- Regulations interpreted to prohibit a manufacturer from speaking to healthcare professionals about on-label uses of a drug in a setting where physicians may prescribe the drug for both on-label and off-label uses.
Par Pharmaceutical v. FDA (2011)

- Declaratory action dismissed as a condition of Par’s settlement with the Department of Justice in 2013.
United States v. Caronia (2012)

• “The FDA . . . has concluded that ‘[a]n approved drug that is marketed for an unapproved use (whether in labeling or not) is misbranded because the labeling of such drug does not include ‘adequate directions for use.’ . . . Thus, the government has treated promotional speech as more than merely evidence of a drug's intended use — it has construed the FDCA to prohibit promotional speech as misbranding itself.”

Judge Denny Chin (2d Cir.)

703 F.3d at 155
United States v. Caronia (2012)

• “The government's construction of the FDCA essentially legalizes the outcome — off-label use — but prohibits the free flow of information that would inform that outcome. If the government's objective is to shepherd physicians to prescribe drugs only on-label, criminalizing manufacturer promotion of off-label use while permitting others to promote such use to physicians is an indirect and questionably effective means to achieve that goal.”

703 F.3d at 167
The Government’s Post-\textit{Caronia} Approach
A “nightmare”

“If [Caronia] were to change the situation so that yes, people had to get their first claim in with adequate and well-controlled studies, but after that they didn’t have to bother anymore, and if that made them not bother anymore, that would be a nightmare.”

-Robert Temple, Deputy Director for Clinical Science, FDA’s Center for Drug Evaluation and Research (December 2012)
No significant effect

“FDA does not believe that the *Caronia* decision will significantly affect the agency’s enforcement of drug misbranding provisions of the Food, Drug, and Cosmetic Act.”

- Tom Abrams, Director, Office of Prescription Drug Promotion, FDA Center for Drug Evaluation and Research (January 2013)
“I don’t think you want to test it”

“When I think of all the prosecutions we’ve done in my office, I can’t think of any that would be covered by the Caronia decision . . . I don’t think you want to test it.”

- Carmen Ortiz, U.S. Attorney for the District of Massachusetts (January 2013)
## Post-Caronia Off-Label Promotion Settlements

<table>
<thead>
<tr>
<th>Date</th>
<th>Company</th>
<th>Amount</th>
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<tbody>
<tr>
<td>December 12, 2012</td>
<td>Pfizer</td>
<td>$55 million</td>
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<tr>
<td>December 19, 2012</td>
<td>Amgen</td>
<td>$762 million</td>
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<td>March 15, 2013</td>
<td>Par Pharmaceutical</td>
<td>$45 million</td>
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<td>May 24, 2013</td>
<td>ISTA Pharmaceuticals</td>
<td>$33.5 million</td>
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<tr>
<td>July 30, 2013</td>
<td>Wyeth</td>
<td>$490.9 million</td>
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First Amendment Principles
Central Hudson and Commercial Speech

“The First Amendment . . . protects commercial speech from unwarranted governmental regulation. Commercial expression not only serves the economic interest of the speaker, but also assists consumers and furthers the societal interest in the fullest possible dissemination of information.”

Central Hudson and Commercial Speech

- If commercial speech relates to lawful activity and is not false or misleading, the government may not restrict it unless:
  - The regulation serves a substantial interest
  - The regulation directly advances the asserted interest (not ineffective or remote)
  - The regulation does not restrict more speech than necessary to serve the interest
Virginia State Board of Pharmacy v. Virginia Citizens Consumer Council

“It is precisely this kind of choice, between the dangers of suppressing information, and the dangers of its misuse if it is freely available, that the First Amendment makes for us.”

425 U.S. at 770
44 Liquormart, Inc. v. Rhode Island

• The government’s “paternalistic assumption that the public will use truthful, nonmisleading commercial information unwisely cannot justify a decision to suppress it.”

Justice John Paul Stevens

517 U.S. at 497
Thompson v. Western States Medical Center

“We have previously rejected the notion that the Government has an interest in preventing the dissemination of truthful commercial information in order to prevent members of the public from making bad decisions with the information.”

535 U.S. at 374
Supreme Court Trend

• Protection of speech generally, including commercial speech
Supreme Court Trend  
(October 2009-Present)

<table>
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<tr>
<th>Case Name</th>
<th>Speech Protected</th>
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<tr>
<td>U.S. Agency for International Development v. Alliance for Open Society International</td>
<td>✓</td>
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<tr>
<td>United States v. Alvarez</td>
<td>✓</td>
</tr>
<tr>
<td>Federal Communications Commission v. Fox Television Stations</td>
<td>*Did not decide</td>
</tr>
<tr>
<td>Knox v. Service Employees International Union</td>
<td>✓</td>
</tr>
<tr>
<td>Snyder v. Phelps</td>
<td>✓</td>
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<tr>
<td>Brown v. Entertainment Merchants Association</td>
<td>✓</td>
</tr>
<tr>
<td>Sorrell v. IMS Health</td>
<td>✓</td>
</tr>
<tr>
<td>Arizona Free Enterprise Club’s Freedom Club PAC v. Bennett</td>
<td>✓</td>
</tr>
<tr>
<td>Christian Legal Society v. Martinez</td>
<td>✗</td>
</tr>
<tr>
<td>Citizens United v. Federal Election Commission</td>
<td>✓</td>
</tr>
<tr>
<td>United States v. Stevens</td>
<td>✓</td>
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“[T]he FEC has created a regime that allows it to select what political speech is safe for public consumption by applying ambiguous tests. If parties want to avoid litigation and the possibility of civil and criminal penalties, they must either refrain from speaking or ask the FEC to issue an advisory opinion approving of the political speech in question . . . . This is an unprecedented governmental intervention into the realm of speech.”

130 S. Ct. at 896

“[T]he First Amendment protects against the Government; it does not leave us at the mercy of noblesse oblige. We would not uphold an unconstitutional statute merely because the Government promised to use it responsibly.”

130 S.Ct. at 1591
“Speech is powerful. It can stir people to action, move them to tears of both joy and sorrow, and—as it did here—inflict great pain. On the facts before us, we cannot react to that pain by punishing the speaker. As a Nation we have chosen a different course—to protect even hurtful speech on public issues to ensure that we do not stifle public debate.”

131 S. Ct. at 1220
“The State may not burden the speech of others in order to tilt public debate in a preferred direction. ‘The commercial marketplace, like other spheres of our social and cultural life, provides a forum where ideas and information flourish. Some of the ideas and information are vital, some of slight worth. But the general rule is that the speaker and the audience, not the government, assesses the value of the information presented.’”

Justice Anthony Kennedy

131 S. Ct. at 2672
The Path Forward
Substantial Governmental Interests

• Ensuring that physicians receive truthful and non-misleading information so that they may make informed treatment decisions
• Providing manufacturers with incentives to get new uses on label
• Ensuring that products are safe and effective for the conditions for which physicians prescribe them
More Restrictive than Necessary?
Medical Information Working Group
Medical Information Working Group

• Comments
  – CDER’s Medical Policy Council (2013)

• Citizen Petitions
  – July 2011 (comments to docket in 2013)
  – September 2013
Other Approaches

• Self-regulation:
  – Prescription Medicines Code of Practice Authority
  – PhRMA Code
  – Corporate Codes of Conduct
QUESTIONS?

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